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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/737,457	03/12/1997	DONALD LEONARD NICHOLAS CARDY	960670.ORI	5220

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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 05/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/737,457	CARDY ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/29/03, 5/8/03, 3/1/04, 3/4/04, 7/9/04*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-7,9,11,16-19 and 21-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-7,9,11,16-19 and 21-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. In response to the amendment filed 4/24/02, an additional restriction election was required under 35 U.S.C. § 121 as set forth in the paper mailed 10/07/02.

Applicant's election of Group I, with traverse, drawn to a polypeptide comprising a ScFv, a p53 fragment (KYICNSSCM, SEQ ID NO:7), and optionally, an HIV tat protein translocation domain, in the paper filed 10/03/02 is acknowledged. Upon reconsideration, and in view of the cancellation of the subject matter of Groups II and IV, in the paper filed 7/09/04, the method of Group III has been rejoined.

2. Claims 1, 2, 5-7, 9, 11, 16-19, and 21-23 are pending and being acted upon.

3. In view of Applicant's amendments and responses, the previous rejections under 35 U.S.C. 112, first paragraph, for the introduction of new matter, have been withdrawn. Additionally, the rejection under 35 U.S.C. 103(a) has been withdrawn because the Casten et al. reference does not teach the use of a scFv.

4. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 21-23 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons set forth previously in the paper mailed 6/13/00.

6. Applicant's arguments, filed 4/24/02, have been fully considered but have not been found convincing. Applicant argues that the amending of Claim 21 to recite a method of "stimulating cell lysis" rather than a method of "modulating the immune response" overcomes the previous rejection.

It is the Examiner's position that even as amended, the specification cannot sufficiently enable the breadth of the claimed method. Note that the method now encompasses an *in vivo* method of generic stimulation of cell lysis, i.e., a method of stimulating the lysis of *any* cell, *anywhere*, in *any* subject, apparently indiscriminately. Clearly, the specification cannot enable such a method with the limited disclosure of just two specific *in vitro* ^{51}Cr release assays. Said disclosure cannot be considered to be commensurate in scope with the method of the instant claims.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 6 and 7 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the term "modulate" has not been defined in the specification; as the term might encompass responses ranging from increased or decreased production of a cytokine to apoptosis, said term is considered vague and indefinite, absent a specific definition.

Applicant has not addressed this rejection.

9. The following are new grounds of rejection necessitated by Applicant's amendment.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1, 2, 5-7, 9, 11, 16-19, and 21-23 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Casten et al. (1988), in view of Fawell et al. (1994), Noguchi et al. (1994), and U.S. Patent No. 6,172,197.

Casten et al. teach a chimeric polypeptide for lysing cells (and a method of same) comprising a binding portion comprising at least a portion of an Fab immunoglobulin fragment having specific binding affinity for a eukaryotic target cell surface component (MHC Class I or Class II receptors) and an effector portion consisting of at least one copy of an immunogenic peptide whereby binding of the polypeptide induces internalization to allow presentation of the effector by the MHC of the target cell(see particularly page 173 paragraph 2).

The reference teaching differs from the claimed invention in that it does not teach an antibody comprising a scFv, nor the use of an HIV tat translocation portion, nor does it teach a p53 effector portion.

Fawell et al. teach the use of the HIV tat protein for cellular translocation (see particularly page 668, second paragraph). They teach that HIV tat can be used as a "generic" translocation signal to "efficiently deliver heterologous molecules into cells" (page 664, paragraph 3).

Noguchi et al. teach the use of p53 as an "obvious candidate for T cell recognition" because the gene is "frequently mutated in tumors of experimental animals and humans" (see particularly page 3171, first column, second paragraph and pages 3173-3174, Discussion).

The '197 patent teaches that Fab fragments and scFv are essentially interchangeable, i.e., they are equivalent compositions, however scFvs have the added advantage of being recombinantly producible from a single protein chain (see particularly column 1, line 54 - column 2, line 8).

From the teachings of the references it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the Fab-effector chimeric polypeptide and use said polypeptide for lysing cells, as taught by Casten et al., by the addition of an HIV tat translocation domain, as taught by Fawell et al., and combine it with a p53 effector portion, as taught by Noguchi et al. One of ordinary skill in the art would have been motivated to refine the internal cellular targeting of the chimeric antibody of Casten et al. with the generic translocation component, as taught by

both Fawell et al., "to efficiently deliver heterologous molecules into cells", and modify the effector component to display various effectors, including p53, because p53 is "frequently mutated in tumors of experimental animals and humans", as taught by Noguchi et al., is an obvious choice as a protein to be presented by MHC for immune system targeting. Additionally, the substitution of an scFv for the Fab taught by Casten et al. would have been obvious given the teachings of the '197 patent that Fab fragments and scFv are essentially interchangeable, i.e., they are equivalent compositions, however scFvs have the added advantage of being recombinantly producible from a single protein chain.

12. Claims 1, 2, 5-7, 9, 11, 16-19, and 21-23 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) an effector portion comprising KYICNSSCM (SEQ ID NO:7), a signal derived from HIV tat protein (Claims 1 and 2).

B) a method to induce cell lysis (Claim 2) or a method of stimulating cell lysis (Claim 21).

C) a method comprising … a target cell (Claims 22 and 23).

Applicant's amendment, filed 4/24/02, asserts that no new matter has been added.

Regarding A), the specification does not generically teach the use of an effector portion comprising KYICNSSCM (SEQ ID NO:7), the specification only teaches the use of the portion in the specific context of Example 1. Additionally, the specification supports only a signal derived from HIV-1 tat protein.

Regarding B), the specification does not teach a generic method of inducing or stimulating cell lysis.

Regarding C), the specification does not teach a generic method comprising a target cell.

13. Claims 21-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

A) a method of stimulating cell lysis of a human or animal subject… (Claim 21) seems nonsensical as it appears that the intent of the claim is to lyse an entire subject.

B) "the target cell" of Claim 22 has no antecedent basis in Claim 21.

14. Applicant's amendment or action necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

17. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications

is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Inquiries of a general nature may also be directed to the Technology Center 1600 Receptionist at (571) 272-1600.

5/18/05

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